THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH WITH OPTIONAL PROCEDURES

AL101 prior to standard-of-care surgery in patients with Notch activated adenoid cystic carcinoma (ACC)

2021-0296

Subtitle: AL101 V1

Study Chair: Renata Ferrarotto

_____ _____
Participant's Name Medical Record Number

This is an informed consent and authorization form for a research study. It includes a summary about the study. A more detailed description of procedures and risks is provided after the summary.

This study is funded by the Department of Defense (DoD).

This research has been reviewed and approved by an Institutional Review Board (IRB - a committee that reviews research studies).

STUDY SUMMARY

The goal of this clinical research study is to learn if AL101 (also called BMS-906024) can help to control adenoid cystic carcinoma (ACC) that has a NOTCH pathway activation. The safety of this drug will also be studied.

This is an investigational study. AL101 is not FDA approved or commercially available. It is currently being used for research purposes only. The study doctor can explain how AL101 is designed to work.

AL101 may help to control the disease. Future patients may benefit from what is learned. There may be no benefits for you in this study.

Your participation is completely voluntary. Before choosing to take part in this study, you should discuss with the study team any concerns you may have, including side effects,

potential expenses, and time commitment. If you take part in this study, you may experience diarrhea, nausea, and/or fatigue. There will be weekly doses, so you may have lodging/travel costs if you do not live in the area. You should also know that taking part in this study may lead to a delay in or inability to receive therapy that may be curative, such as surgery.

You can read a full list of potential side effects below in the Possible Risks section of this consent.

You will receive study drug weekly for 6 to 8 weeks before surgery. After surgery, you may be able to continue receiving it for as long as the study doctor thinks it is in your best interest.

AL101 will be provided at no cost to you while you are on study.

You may choose not to take part in this study. Instead of taking part in this study, you may choose to receive other approved drugs, surgery, and/or radiation therapy. You may choose to receive other investigational therapy, if available. The doctor will discuss these treatment options with you, including their risks and benefits. You may choose not to have treatment for cancer at all. In all cases, you will receive appropriate medical care, including treatment for pain and other symptoms of cancer.

1. STUDY DETAILS

Screening Tests

Signing this consent form does not mean that you will be able to take part in this study. The following screening tests will help the doctor decide if you are eligible:

- You will have a physical exam.
- You will have an EKG to check your heart function.
- Blood (about 2 tablespoons) will be drawn for routine tests and blood clotting tests.
- Blood (about 2 teaspoons) will be drawn for biomarker testing. Biomarkers are found in the blood/tissue and may be related to your reaction to the study drug.
- You will have a biopsy for biomarker testing. The study doctor will discuss the procedure with you in more detail.
- You will have an MRI or CT scan to check the status of the disease.
- Leftover tumor tissue from a previous surgery or biopsy will be collected to check the status of the disease and to check for the presence of NOTCH protein.
- If you can become pregnant, urine will be collected for a pregnancy test. To take part in this study, you must not be pregnant.

The study doctor will discuss the screening test results with you. If the screening tests show that you are not eligible to take part in the study, you will not be enrolled. Other treatment options will be discussed with you.

Up to 14 participants will be enrolled in this study. All will take part at MD Anderson.

Study Drug Administration

If you are found to be eligible to take part in this study, you will receive AL101 by vein over about 1 hour on Days 1, 8, 15, and 22 of each 28-day cycle. There will be 2 cycles. You will receive drugs for 6 to 8 weeks before your scheduled surgery.

You will be given standard drugs to help decrease the risk of side effects. You may ask the study staff for information about how the drugs are given and their risks.

You will then have your scheduled surgery as part of your standard of care. You will receive a separate consent form for this procedure.

After surgery, if the study doctor thinks it is in your best interest, you may continue receiving the study drug weekly.

You will no longer be able to take the study drug if the disease gets worse, if intolerable side effects occur, or if you are unable to follow study directions.

Study Visits

On **Day 1 of each cycle:**
- You will have a physical exam.
- Blood (about 3-4 tablespoons) will be drawn for routine tests.
- Blood (about 1 teaspoon each time) will be drawn for pharmacokinetic (PK) testing before the dose of the study drug and 2 times over the 7 hours after the dose (Cycle 1 only).
- Blood (about 2 teaspoons) will be drawn for biomarker testing (Cycle 1 only).

On **Days 8 and 22 of Cycle 1:**
- You will have a physical exam.
- Blood (about 5 teaspoons) will be drawn for routine tests, PK testing, and biomarker testing.

On **Day 15 of Cycle 1 and Cycle 2 and Day 8 of Cycle 2:**
- You will have a physical exam.
- Blood (about 3-4 tablespoons) will be drawn for routine tests.

On **Day 22 of Cycle 2:**
- You will have a physical exam.
- Blood (about 2 teaspoons) will be drawn for routine tests and blood clotting tests.
- Blood (about 1 teaspoon each time) will be drawn for PK testing before the dose and 2 times over the 7 hours after the dose.
- Blood (about 1 teaspoon) will be drawn for biomarker testing before and 7 hours after the dose of the study drug.
- You will have an MRI or CT scan to check the status of the disease.

On **the day of surgery,** blood (up to 2 teaspoons) will be drawn for PK and biomarker testing within 4 hours of surgery. Tumor tissue removed during surgery will also be used for biomarker testing.

If you continue receiving the drug after surgery, you will have study visits every week.

On **Days 1, 8, 15, and 22 of every cycle after surgery**:
- Blood (about 2 teaspoons) will be drawn for routine tests.
- You will have a physical exam (Days 1 and 15 only).

Additionally, **every 8 weeks**, you will have an MRI or CT scan to check the status of the disease.

End of Treatment Visit
Within 6 weeks after surgery, or within 30 days after your last dose of AL101 (if you continue receiving it after surgery:
- You will have a physical exam.
- Blood (about 2 teaspoons) will be drawn for routine tests.
- Blood (about 2 teaspoons) will be drawn for biomarker testing.

You may be called or emailed every 6 months after the end-of-treatment visit and asked about how you are doing. Each call would last about 5-10 minutes.

Other Information
While you are in the study, you must:
- Follow all instructions given to you by the study doctor and the study staff
- Come to the study site for all scheduled visits
- Agree to have all the testing required by the study protocol
- Tell the study doctor or study staff about any changes in your overall health or any side effects you are having
- Tell the study doctor or study staff about any medications you are taking
- Tell the study doctor or study staff if you want to stop being in the study

2. POSSIBLE RISKS

While on this study, you are at risk for side effects. You should discuss these with the study doctor. The more commonly occurring side effects are listed in this form, as are rare but serious side effects. You may also want to ask about uncommon side effects that have been observed in small numbers of patients but are not listed in this form. Many side effects go away shortly after treatment is stopped, but in some cases side effects may be serious, long-lasting or permanent, and may even result in hospitalization and/or death.

Side effects will vary from person to person, and some may occur after you have stopped receiving treatment. Tell the study staff about any side effects you may have, even if you do not think they are related to the study drug/procedures.

AL101 Side Effects

This is an early study of AL101, so the side effects are not well known. Based on early human studies, AL101 may cause:

• difficulty sleeping • skin rash • itching • dry/cracking/bleeding skin • abnormal salts, minerals, and/or acids in the blood (possible weakness, swelling, fatigue, low blood pressure, organ failure, heart problems, changes in mental status, and/or seizure)	• nausea/vomiting • diarrhea • abnormal taste • weight loss • hoarse voice • irritation of the lining of the stomach/intestines (possible abdominal pain)	• abnormal liver tests (possible liver damage and/or yellowing of the skin and/or eyes) • liver failure • nosebleed • infusion allergic-like reaction (possible hives, fever, headache, fainting, and/or difficulty breathing)

AL101 may cause you to develop keratoacanthoma, basal cell carcinoma, or squamous cell carcinoma (types of skin cancer). You should wear sunscreen (at least 50 SPF), hat, and UV protective clothing and avoid long periods of exposure to the sun while taking part in this study. Do NOT use tanning beds during or after treatment.

AL101 may cause low blood cell counts (platelets and white blood cells):

- A low platelet count increases your risk of bleeding (such as nosebleeds, bruising, stroke, and/or digestive system bleeding). You may need a platelet transfusion.
- A low white blood cell count increases your risk of infection (such as pneumonia and/or severe blood infection). Infections may occur anywhere and become life-threatening. Symptoms of infection may include fever, pain, redness, and difficulty breathing.

Other Risks

Blood draws may cause pain, bleeding, and/or bruising. You may faint and/or develop an infection with redness and irritation of the vein at the site where blood is drawn. Frequent blood collection may cause anemia (low red blood cell count), which may create a need for blood transfusions.

Having **biopsies** performed may cause pain, bruising, bleeding, redness, low blood pressure, swelling, and/or infection at the site of the biopsies. An allergic reaction to the anesthetic may occur. A scar may form at the biopsy site.

The type of **genetic testing** being performed in this study will not provide you or your doctor information about diseases that are passed down in families. It will not tell the study researchers anything that will prevent you from getting health insurance, and it will

not tell the study researchers anything about any diseases or conditions you may get in the future.

A Federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information when making a decision to hire, promote, or fire you or when setting the terms of your employment.

All health insurance companies and group health plans must follow this law. Be aware that this Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance

CT scans send x-rays through the body at many different angles. You will be exposed to a small dose of radiation. All radiation adds up over a lifetime and may increase the risk of new cancer forming. Some people may feel “closed in” while lying in the scanner. However, the scanner is open at both ends, and an intercom allows you to talk with doctors and staff. If you feel ill or anxious during scanning, doctors and/or radiology technicians will give comfort, or the scanning will be stopped. When a CT scan of the abdominal area is taken, material may be inserted into the rectum to better define the bowel. You will usually drink liquid to help define various abdominal organs. This may cause nausea and/or vomiting. Solution may also be given by vein to make the x-ray pictures more accurate. This may cause an uncomfortable feeling of warmth, nausea, and/or severe allergic reactions. The solution injection may also cause pain, bleeding, bruising, hives, and/or itching.

During the **MRI**, you may feel mild vibrations throughout your body. The machine will produce a loud knocking noise. This is normal. You will be given earplugs to protect your ears. Some people, especially those who tend to feel uncomfortable in small or closed spaces, may feel “closed in” and become anxious while in the scanner. The scanner has an intercom, which will allow you to speak to the staff during the procedure. If you feel ill or anxious during scanning, tell the MRI staff and the scanning will be stopped if you wish. The MRI will require a catheter to be inserted into one of your veins in order to inject the MRI contrast agent. This may cause skin irritation, bleeding, and/or infection. You may have an allergic reaction to the contrast agent.

The magnetic field used in MRI scanning may harm you if you have certain types of metal in your body (as might be found in pacemakers, neurostimulators, or certain clips). It may cause problems with devices, such as pacemakers. If you have metal in your body or devices such as a pacemaker, you should discuss this with the study doctor.

This study may involve unpredictable risks to the participants.

Pregnancy Related Risks
Taking part in this study can result in risks to an unborn or breastfeeding baby, so you should not become pregnant, breastfeed a baby, or father a child while on this study. You must use birth control during the study if you are sexually active. Talk with the study doctor about effective methods to use.

Males: Tell the doctor right away if your partner becomes pregnant or suspects pregnancy. You must use a condom as your method of birth control.

Females: If you are pregnant, you will not be enrolled on this study. If you become pregnant or suspect that you are pregnant, you must tell your doctor right away. The sponsor will ask for information about the pregnancy.

You must practice two effective birth control measures while you are receiving the study drug and for at least 90 days after your last dose of AL101 therapy. The two birth control methods can be either two barrier methods or a barrier method plus a hormonal method to prevent pregnancy. The following are considered adequate barrier methods of birth control: diaphragm, condom, copper intrauterine device, sponge, or spermicide. Appropriate hormonal birth control will include any registered and marketed agent that contains an estrogen and/or a progestational agent (including oral, subcutaneous, intrauterine, or intramuscular agents).

Getting pregnant will result in your removal from this study.

OPTIONAL PROCEDURES FOR THE STUDY

You do not have to agree to the optional procedure in order to take part in this study. There are no benefits to you for taking part in the optional procedure. Future patients may benefit from what is learned. You may stop taking part at any time. There will be no cost to you for taking part in the optional procedure.

Optional Procedure #1: If your tumor tissue is banked (stored) under another research study (such as Lab02-039, Lab03-0320, or 2021-0550) and can be used for biomarker testing, you do not need to have the biopsy at screening. The study doctor will tell you if this applies to you. If this does apply to you and you agree, the banked tissue will be collected and used for biomarker testing, and you will not have the biopsy at screening.

Optional Procedure Risks

There are no expected risks to allowing banked tissue to be collected.

CONSENT/PERMISSION/AUTHORIZATION FOR OPTIONAL PROCEDURES

Circle your choice of “yes” or “no” for each of the following optional procedures:

Optional Procedure #1: If your tumor tissue is banked under another research study, do you agree to allow this tissue to be collected and used for biomarker testing?

YES NO

3. COSTS AND COMPENSATION

If you suffer injury as a direct result of taking part in this study, MD Anderson health providers will provide medical care. However, this medical care will be billed to your insurance provider or you in the ordinary manner. You will not be reimbursed for expenses or compensated financially by MD Anderson or Ayala Pharmaceuticals, Inc. for this injury. You may also contact the Chair of MD Anderson's IRB at 713-792-6477 with questions about study-related injuries. You may also call the study doctor (Dr. Renata Ferrarotto, at 713-792-6363) if you think you have had an injury related to this study. By signing this consent form, you are not giving up any of your legal rights.

Certain tests, procedures, and/or drugs that you may receive as part of this study may be without cost to you because they are for research purposes only. However, your insurance provider and/or you may be financially responsible for the cost of care and treatment of any complications resulting from the research tests, procedures, and/or drugs. Standard medical care that you receive under this research study will be billed to your insurance provider and/or you in the ordinary manner. Before taking part in this study, you may ask about which parts of the research-related care may be provided without charge, which costs your insurance provider may pay for, and which costs may be your responsibility. You may ask that a financial counselor be made available to you to talk about the costs of this study.

Samples that are collected from you in this study may be used for the development of treatments, devices, new drugs, or patentable procedures that may result in commercial profit.

There are no plans to compensate you for any patents or discoveries that may result from your participation in this research.

You may receive $100 per week for up to 8 weeks for taking part in this study.

Additional Information

4. You may ask the study chair (Dr. Renata Ferrarotto, at 713-792-6363) any questions you have about this study. You may also contact the Chair of MD Anderson's Institutional Review Board (IRB - a committee that reviews research studies) at 713-792-6477 with any questions that have to do with this study or your rights as a study participant.

5. You may choose not to take part in this study without any penalty or loss of benefits to which you are otherwise entitled. You may also withdraw from participation in this study at any time without any penalty or loss of benefits. If you

decide you want to stop taking part in the study, it is recommended for your safety that you first talk to your doctor. If you withdraw from this study, you can still choose to be treated at MD Anderson.

6. This study or your participation in it may be changed or stopped without your consent at any time by the study chair, Ayala Pharmaceuticals, Inc., the U.S. Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP), or the IRB of MD Anderson.

7. You will be informed of any new findings or information that might affect your willingness to continue taking part in the study, and you may be asked to sign another informed consent and authorization form stating your continued willingness to participate in this study.

8. MD Anderson may benefit from your participation and/or what is learned in this study.

9. This study is sponsored and/or supported by: Ayala Pharmaceuticals, Inc.

10. In a medical emergency, you may be cared for by someone who has a financial interest with the study sponsor(s)/supporter. If you have any questions about this, you may call the IRB at 713-792-6477.

Future Research

Data

Your personal information is being collected as part of this study. These data may be used by researchers at MD Anderson and Ayala Pharmaceuticals, Inc. and/or shared with other researchers and/or institutions for use in future research.

Samples

Samples (such as blood and/or tissue) are being collected from you as part of this study. Researchers at MD Anderson may use any leftover samples that are stored at MD Anderson in future research.

Before being used or shared for future research, every effort will be made to remove your identifying information from any data and/or research samples. If all identifying information is removed, you will not be asked for additional permission before future research is performed.

If you do not want your samples or data to be used for future research, tell the study doctor. You may withdraw your samples at any time by telling your study team. If you decide to withdraw your samples, they will be returned to the lab they came from or destroyed. However, the data and test results already collected from your samples will be kept and may be used.

In some cases, all of your identifying information may not be removed before your data or research samples are used for future research. If future research is performed at MD Anderson, the researchers must get approval from the Institutional Review Board (IRB) of MD Anderson before your data and/or research samples can be used. At that time, the IRB will decide whether or not further permission from you is required. The IRB is a committee of doctors, researchers, and community members that is responsible for protecting study participants and making sure all research is safe and ethical.

If this research is not performed at MD Anderson, MD Anderson will not have oversight of any data and/or samples.

Genetic Research

Samples collected from you as part of this study will be used for genetic research, which may include whole genome sequencing. Whole genome sequencing is a type of testing in which researchers study your entire genetic makeup (DNA). This may help researchers learn how changes in the ordering of genes may affect a disease or response to treatment. If genetic research is done with your samples, those who have access to those samples may be able to identify you. The results of this research may also be able to be linked to you. A federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that we get from this research when deciding to hire, promote, or fire you or when setting the terms of your employment.

Be aware that this federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. Nor does this federal law prohibit discrimination based on an already known genetic disease or disorder.

Conflict of Interest

Dr. Renata Ferrarotto (Study Chair) has received compensation from Ayala Pharmaceuticals as a Scientific Advisor. The financial interests are within the limits of the conflict of interest policy.

Authorization for Use and Disclosure of Protected Health Information (PHI):

A. During the course of this study, MD Anderson will be collecting and using your PHI, including identifying information, information from your medical record, and

study results. For legal, ethical, research, and safety-related reasons, your doctor and the research team may share your PHI with:

- Federal agencies that require reporting of clinical study data (such as the FDA, National Cancer Institute [NCI], and OHRP)
- The IRB and officials of MD Anderson
- Ayala Pharmaceuticals, Inc., who is a sponsor or supporter of this study, and/or any future sponsors/supporters of the study
- Representatives of the Department of Defense
- Study monitors and auditors who verify the accuracy of the information
- Individuals who put all the study information together in report form

Study sponsors and/or supporters receive limited amounts of PHI. They may also view additional PHI in study records during the monitoring process. MD Anderson's contracts require sponsors/supporters to protect this information and limit how they may use it.

Ayala Pharmaceuticals, Inc. is based in the United States with affiliates in Israel.

In order to participate in this study, the sponsor will need to process certain categories of your personal data. For more information, including how, why, and on what lawful bases Ayala will process your personal data in this study, please read our Clinical Trial Privacy Notice by following the links in the footer of our website at https://www.ayalapharma.com.

B. Signing this consent and authorization form is optional but you cannot take part in this study or receive study-related treatment if you do not agree and sign.

C. MD Anderson will keep your PHI confidential when possible (according to state and federal law). However, in some situations, the FDA could be required to reveal the names of participants.

Once disclosed outside of MD Anderson, federal privacy laws may no longer protect your PHI.

D. The permission to use your PHI will continue indefinitely unless you withdraw your authorization in writing. Instructions on how to do this can be found in the MD Anderson Notice of Privacy Practices (NPP) or you may contact the Chief Privacy Officer at 713-745-6636. If you withdraw your authorization, you will be removed from the study and the data collected about you up to that point can be used and included in data analysis. However, no further information about you will be collected.

E. A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

CONSENT/AUTHORIZATION

I understand the information in this consent form. I have had a chance to read the consent form for this study, or have had it read to me. I have had a chance to think about it, ask questions, and talk about it with others as needed. I give the study chair permission to enroll me on this study. By signing this consent form, I am not giving up any of my legal rights. I will be given a signed copy of this consent document.

_____ _____
SIGNATURE OF PARTICIPANT DATE

_____
PRINTED NAME OF PARTICIPANT

WITNESS TO CONSENT

I was present during the explanation of the research to be performed under this protocol.

_____ _____
SIGNATURE OF WITNESS TO THE VERBAL CONSENT PRESENTATION (OTHER THAN PHYSICIAN OR STUDY CHAIR) DATE
A witness signature is only required for non-English speakers utilizing the short form consent process (VTPS) and patients who are illiterate.

_____
PRINTED NAME OF WITNESS TO THE VERBAL CONSENT

PERSON OBTAINING CONSENT

I have discussed this research study with the participant and/or his or her authorized representative, using language that is understandable and appropriate. I believe that I have fully informed this participant of the nature of this study and its possible benefits and risks and that the participant understood this explanation.

_____ _____
PERSON OBTAINING CONSENT DATE

_____
PRINTED NAME OF PERSON OBTAINING CONSENT

TRANSLATOR

I have translated the above informed consent as written (without additions or subtractions) into_____and assisted the people
(Name of Language)
obtaining and providing consent by translating all questions and responses during the consent process for this participant.

NAME OF TRANSLATOR	SIGNATURE OF TRANSLATOR	DATE

☐

SIGNATURE OF WITNESS TO THE VERBAL TRANSLATION (OTHER THAN TRANSLATOR, PARENT/GUARDIAN, OR STUDY CHAIR)	DATE

PRINTED NAME OF WITNESS TO THE VERBAL TRANSLATION